

Case Report

Rheumatoid arthritis onset after COVID-19 infection: a case report

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ABSTRACT

At the end of 2019, coronavirus disease (COVID-19) outbreak is caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV2). Worldwide researchers and physician try to explore the mechanisms of damage induced by virus, they focus on the short-term and long-term immune-mediated consequences induced by the virus infection. Every day discover a new pathological condition induced by virus and new symptoms and disease may occur after recovery from disease. Our case report is 41 years old, Indian lady who presented to our primary health care centre complaining of multiple small hand joints pain, both elbows and knees pain with swelling of them and prolonged morning stiffness, diagnosed seropositive rheumatoid arthritis (RA) (arthritis, positive rheumatoid factor (RF), and X-ray changes) after 1 month recovery from COVID-19 infection. She did not have any joint pain and she had negative RF before COVID-19 infection with no family history of RA.

Keywords: Rheumatoid arthritis, COVID-19, Rheumatic factor, Polyarthritis, Corona infection

INTRODUCTION

At the end of 2019, a novel coronavirus, was the leading cause for a cluster of pneumonia and chest infection in China; the infection rapidly spread throughout the world, resulting in a global pandemic. The virus name is severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and the illness name is coronavirus disease 2019 (COVID-19). The infection with COVID-19 in adults varies from asymptomatic condition to mild symptoms of respiratory tract infection to severe pneumonia with acute respiratory distress syndrome (ARDS) and multiple organ failure and dysfunction. Our understanding of the COVID-19 spectrum and optimal management strategies continues to evolve.¹

COVID-19 infection which is caused by SARS-CoV-2 virus, can lead to severe inflammation and one of suggestion is induce autoimmune phenomena. Many studies focusing on immune-mediated consequences have recorded autoantibodies in patients with COVID-19,

particularly anti-cardiolipin, anti- β 2-glycoprotein I and antinuclear antibodies.^{2,3}

The flaring of rheumatoid arthritis (RA) and detection of anti-citrullinated protein antibodies (ACPA) and rheumatic factor (RF) after SARS-Cov-2 infection have also been described.^{1,4} Despite the fact, it is unclear how often ACPA occur after COVID-19 and if it is differ from ACPA possible present in patients with RA.

Most of severe cases expressed to be related to pro-coagulant state and by an inflammatory cytokine storm same to one present in macrophage activation syndrome.⁵⁻⁷ The hyperimmune response absolutely contributes to the severe damage caused by COVID-19 infection and possible initiate autoimmune processes in predisposed people.⁸ Viral infections are expected to be connected in pathogenesis of many rheumatologic diseases and some cases of autoimmune-induced diseases after virus SARS-CoV2 infection are documented in some literature.^{9,10}

Despite COVID-19 is not yet regarded as a trigger factor for RA, this similarity has led to the doubt that COVID-19 might be a risk factor for deducing a RA flare.⁴

In this case report we will highlight post-SARS-CoV2 infection arthritis with patient was negative for rheumatoid arthritis before infection which may occur as a new pathological condition related to COVID-19.

CASE REPORT

A 41 years old, Indian lady who presented to our primary health care centre complaining of multiple small hand joints pain, also pain in both elbows and knees, with swelling of them and prolonged morning stiffness without comorbidity after 1 month from COVID infection.

Her story start in 21 April 2020, when diagnosed with COVID-19 infection. At that time she came to health center complain from hyperpyrexia, headache, asthenia, malaise, shortness of breath and sore throat for three days. A nasopharyngeal swab for polymerase chain reaction (PCR) SARS-CoV-2 was positive, and the patient was diagnosed with COVID-19. After 4 days on 25 April 2020, she did chest X ray shows bilateral lung infiltrate and diagnose as COVID-19 pneumonia, she had normal electrocardiography (ECG), her blood test shown in Table 1.

Table 1: Laboratory investigation result after 5 days from diagnosis COVID-19 infection with normal range and comments.

Laboratory test	Level	Normal range	Comment
WBC	6 x10 ³ /ul	4-10	Normal
Hgb	7.9 gm/dl	12.0-15.0	Low
MCV	53.3 fl	83-101.0	Low
MCH	26 gm/dl	27.0-32.0	Normal
ESR	15	0-15	Normal
D-Dimer	0.28 mg/l	0-0.44	Normal
CRP	0.8 mg/l	0-5	Normal
Platelet	304x10 ³ /ul	150-400	Normal
Ferittin	24	8-252	Normal

She admitted to a provisional COVID-19 hospital treated with intravenous antibiotics ceftriaxone (2 g per day for 3 days), azithromycin (500 mg, oral, capsule daily for 10 day), lopinavir/ritonavir, 2 tablets, oral, twice daily for 14 day, hydroxychloroquine, 400 mg, oral, tablet, daily for 10 days and paracetamol, 1,000 mg, oral, tablet when necessary. After 5 days discharge from hospital and transfer to quarantine for 20 days till she get nasopharyngeal -PCR for SARS-CoV-2 test negative on 31 May 2020 (it was positive through all quarantine days as it repeated weekly).

After one month from recovery from covid infection she start to have pain and swelling of many joints in hands,

wrists, elbows, shoulders, knee and ankles. In addition she had morning stiffness express as difficulty or slowness in moving of the joints at morning more than 30 minutes need to start normal joint movements. This stiffness improve with movements. Also she had generalized body aching and fatigue, with low-grade fever, mild weight loss with normal appetite. There is no family history of RA, she is not smoker not alcoholic. She consulted physicians many time and reassured her after she did SARS-CoV-2 test negative repeated twice in June 2021.

After 6 weeks, patient consulted us at the primary health care center on 7 July 2020 with same above complain, her physical examination of upper extremity joints were tender to the touch and restricted range of movement with swelling and little warmer for the following joints: small joints of the hands like metacarpophalangeal (MCP) and proximal interphalangeal (PIP) joints of the all fingers, the interphalangeal joints of the thumbs, wrist, elbow of both sides. Also inability to make a fist in hand with reduced grip strength of the hands and wrists with little loss of wrist extension. There is no joint deformities, no subcutaneous nodules.

Physical examination of lower extremity of forefoot and ankles: there is tenderness and mild swelling of metatarsophalangeal joints (MTP joints) and proximal interphalangeal joints of toes in a pattern that mirrors in the hand, normal ankle and knee joint.

Her rheumatology work up shown in Table 2.

Table 2: Laboratory investigation result after 5 weeks from COVID-19 infection recovery.

Laboratory test	Level	Normal range	Comment
Rheumatoid factor	22 IU/ml	0-14	High
Anti-cyclic citrullinated peptide	20 U/ml	0-17	High
Anti-nuclear antibodies	Negative		
C3 complement	26 gm/dl	27.0-32.0	Normal
ESR	44	0-15	High
CRP	20 mg/l	0-5	Normal
HLA B27 (human leukocyte antigen)	Negative	Negative	

Her X-ray of both hands and wrist (anteroposterior (AP) and oblique) views shows osteopenic texture of the carpal bones as well as the juxta-articular regions, radiological sign for early RA, for further assessment and laboratory investigation and follow up.

No evidence of obvious displaced fracture seen. Bony fair alignment is preserved.

She achieved total score of 8 (out of 10) from the individual scores in four domains according to 2010 ACR/EULAR criteria (American college of rheumatology criteria used to diagnose RA) present in Appendix.^{11,12}

Then we referred her to rheumatology clinic and there diagnose her as seropositive RA depending on clinical presentation, blood test result and radiological changes of hand X ray (arthritis, positive RF, X-ray changes) with no oral or genital ulcers, no fever, no Raynaud's phenomena, no muscle weakness, no skin rash, no dry eyes.

Management plan

They treated her with methotrexate 15 mg weekly and methylprednisolone acetate depot 40 mg/ml once after 1 month patient still had multiple joint pain of small hand joints, both elbows and knees with swelling with prolonged morning stiffness. Then patient is managed with oral methotrexate 15 mg weekly, folic acid 5 mg oral daily, hydroxychloroquine 200 mg daily and oral prednisolone 5 mg twice per day and respond.

After few months in January 2021 she developed another flare up, having small hand joint pain, swellings her RF positive and C-reactive protein (CRP) and erythrocytic sedimentation rate (ESR) 18. Her rheumatology physician start oral tofacitinib 5 mg twice daily (which is biologic DMARDs – drugs classified as disease-modifying ant rheumatic drugs) and increase methotrexate to 20 mg weekly, they stopped hydroxychloroquine as patient cannot tolerate it. Her symptoms improve on biological treatment. After 2 months get another flare up of RA symptoms demonstrate by joint swelling, redness and pain (with other sign of inflammation and elevated ESR and CRP), her rheumatologist specialist physician change medication to given glomumab 50 mg (which is biologic DMARDs) subcutaneous every month and reduce methotrexate to 7.5 mg every week due to elevated liver enzymes and add prednisolone tablet for short time. After that her symptoms improve and for last 4 months she is on last medication and under control.

DISCUSSION

SARS-CoV-2 infection is one of mysterious new disease that is not restricted by severity of infection itself, but about the consecutive disease could be followed after curing from it.⁸ One of these disease would like to highlighted in this case report is seropositive rheumatoid arthritis (positive RF) with little elevation anti cyclic citrullinated peptide (ACCP) and how patient suffer from symptoms till diagnosed and treated. The early discover of disease (RA) is really reflecting on the progressiveness of disease, kind of management, and flare up of it.¹¹ This patient was treated with recommended protocol of treatment for COVID-19 at that time and cured.⁵ Nearly, about one month after the resolution of COVID-19 infection, this lady suffers from arthritis symptoms. Later after diagnosis, she responds to methotrexate,

corticosteroids and biological medication, with approximately decrease joint disease.

Even though, rheumatoid arthritis possible happened as coincidence after COVID-19 infection, rather than connected to it.¹⁴ We cannot conclude that especially our patient does not have any family history for RA and her rheumatic factor and other inflammatory markers were negative before. Also, this case report diagnosed at beginning of COVID-19 pandemic and at that time no information available about the consequences of disease. Moreover, the relation between COVID-19 and the onset of arthritis has been previously documented in one article.¹³

CONCLUSION

This case report might evoke that SARS-CoV-2 was engaged in initiate rheumatoid arthritis with rheumatic factor positive. But we cannot remove the possibility that the onset of this arthritis could be occur by chance. However, other reports mention that, the presence of autoantibodies after SARS-CoV-2 infection might imply that this virus could also act as a trigger of joint arthritis or other autoimmune diseases. Long-term follow up of patients infected by COVID-19 might prepare an answer to this challenging question. SARS-CoV2 considered as a new devastating entity and need study on worldwide scale.

Recommendations

Recommendation of authors is to take in consideration any symptoms appear after COVID-19 infection and not consider as chronic fatigue after viral infection. Also to observe patient after cure to detect any other new disease possible appear after this new virus infection.

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APPENDIX

The 2010 American College of Rheumatology/European league against rheumatism classification criteria for RA.^{11,12}

S. no.	Questions
1	Target population (who should be tested?): patients who
a	have at least one joint with definite clinical synovitis (swelling)*
b	with the synovitis not better explained by another disease†
2	Classification criteria for RA (score-based algorithm: add score of categories A through D; a score of ≥ 6 out of 10 is needed for classification of a patient as having definite RA)‡
A	Joint involvement§
a	One large joint - 0
b	Two to 10 large joints - 1
c	One to three small joints (with or without involvement of large joints)¶ - 2
d	Four to 10 small joints (with or without involvement of large joints) - 3
e	>10 joints (at least one small joint)** - 5
B	Serology (at least one test result is needed for classification)††
a	Negative RF and negative ACPA - 0
b	Low positive RF or low positive ACPA - 2
c	High positive RF or high positive ACPA - 3
C	Acute phase reactants (at least one test result is needed for classification)‡‡
a	Normal CRP and normal ESR - 0
b	Abnormal CRP or normal ESR - 1
D	Duration of symptoms§§
a	<Six weeks - 0
b	\geq Six weeks - 1

ACPA=anti-citrullinated protein antibody; CRP=C-reactive protein; ESR=erythrocyte sedimentation rate; RA=rheumatoid arthritis. *—The criteria are aimed at classification of newly presenting patients. In addition, patients with erosive disease typical of RA with a history compatible with prior fulfillment of the 2010 criteria should be classified as having RA. Patients with long-standing disease, including those whose disease is inactive (with or without treatment), who, based on retrospectively available data, have previously fulfilled the 2010 criteria should be classified as having RA. †—Differential diagnoses differ in patients with different presentations, but may include conditions such as systemic lupus erythematosus, psoriatic arthritis, and gout. If it is unclear about the relevant differential diagnoses to consider, an expert rheumatologist should be consulted. ‡—Although patients with a score of less than 6 out of 10 are not classifiable as having RA, their status can be reassessed, and the criteria might be fulfilled cumulatively over time. §—Joint involvement refers to any swollen or tender joint on examination, which may be confirmed by imaging evidence of synovitis. Distal interphalangeal joints, first carpometacarpal joints, and first metatarsophalangeal joints are excluded from assessment. Categories of joint distribution are classified according to the location and number of involved joints, with placement into the highest category possible based on the pattern of joint involvement. ||—“Large joints” refers to shoulders, elbows, hips, knees, and ankles. ¶—“Small joints” refers to the metacarpophalangeal joints, proximal interphalangeal joints, second to fifth metatarsophalangeal joints, thumb interphalangeal joints, and wrists. **—In this category, at least one of the involved joints must be a small joint; the other joints can include any combination of large and additional small joints, as well as other joints not specifically listed elsewhere (e.g. temporomandibular, acromioclavicular, sternoclavicular). ††—Negative refers to international unit values that are less than or equal to the upper limit of normal for the laboratory and assay; low positive refers to international unit values that are higher than the upper limit of normal but three or less times the upper limit of normal for the laboratory and assay; high positive refers to international unit values that are more than three times the upper limit of normal for the laboratory and assay. When rheumatoid factor information is only available as positive or negative, a positive result should be scored as low positive for rheumatoid factor. ‡‡—Normal/abnormal is determined by local laboratory standards. §§—Duration of symptoms refers to patient self-report of the duration of signs or symptoms of synovitis (e.g. pain, swelling, tenderness) of joints that are clinically involved at the time of assessment, regardless of treatment status.